REMARKS

I. Introduction

Receipt of a non-final Office Action dated April 19, 2006, is acknowledged. In the Action, the claims are rejected as allegedly failing to meet the written description requirement.

The claims are also rejected as allegedly obvious over Liversidge *et al.*, U.S. Patent No. 5,145,684 ("Liversidge"), in view of Folke Moren, AEROSOLS IN MEDICINE, PRINCIPLES, DIAGNOSIS AND THERAPY, Chapter 13, pp. 321-350, Elsevier Science Publisher (1993) ("Moren"), or in view of A.R. Gennaro, REMINGTON'S PHARMACEUTICAL SCIENCES, 17TH ED., Chapter 93, pp. 1670-77 (1985) ("Gennaro") and Dieter Kohler, AEROSOLS IN MEDICINE, PRINCIPLES, DIAGNOSIS AND THERAPY, Chapter 12, pp. 303-19, (1993) ("Kohler").

Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

II. Status of the Claims

Claims 28-40, 42-45, and 47-59 are pending and under examination. No amendments to the claims have been made.

III. Rejection of the Claims Under 35 U.S.C. § 112, 1st Paragraph

Claims 28-40, 42-45, and 47-59 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to meet the written description requirement. In particular, the claims are rejected because the phrase "method of delivering" is allegedly not found in the specification. Applicants respectfully traverse this ground for rejection.

As outlined in Applicants' response to a January 21, 2004 Office Action dated February 4, 2004, the support for a claim directed to a method of delivering an aerosol to the lungs can be found on page 2, line 35, through page 3, line 5. But for the Examiner's convenience, the claim chart previously presented is reproduced below.

Claim 28	Exemplary Support in the Application
28. A method of delivering an aerosol to the lungs of a mammal comprising the steps of:	"In yet another aspect of the invention, there is provided a method of treating a mammal comprising the steps of: . . . b) administering said aerosol to the respiratory system of said mammal." (Page 2, line 35, through page 3, line 5)
(a) providing an aerosol composition, wherein said composition comprises aqueous droplets	"there is provided a method of treating a mammal comprising the steps of: a) forming an aerosol of an aqueous dispersion . . ." (Page 2, line 35, through page 3, line 1.)
having a particle size of less than about fifty microns in diameter,	"The droplets in the aerosols typically have a size less than about 50 microns in diameter . . ." (Page 3, lines 18-19.)
wherein the aqueous droplets comprise: (i) water,	"there is provided a method of treating a mammal comprising the steps of: a) forming an aerosol of an aqueous dispersion of nanoparticles,
(ii) crystalline particles of a therapeutic agent	"there is provided a method of treating a mammal comprising the steps of: a) forming an aerosol of an aqueous dispersion of nanoparticles, said nanoparticles comprising insoluble therapeutic agent particles . . ." (Page 2, line 35, through page 3, line 2.) "The therapeutic or diagnostic agent exists as a discrete, crystalline phase." (Page 4, lines 11-12.)
which is poorly soluble in water,	"The therapeutic or diagnostic agent must be poorly soluble and dispersible in at least one liquid medium. . . A preferred liquid dispersion medium is water." (Page 4, lines 17-21.)
wherein the crystalline particles have a submicron particle size; and	In a particularly preferred method, a therapeutic or diagnostic agent is prepared in the form of submicron particles . . . (Page 13, lines 14-15.) "The coarse therapeutic or diagnostic agent selected can then be added to a liquid medium in which it is essentially insoluble to form a premix. . . .The premix can be used

Claim 28	Exemplary Support in the Application
	directly by subjecting it to mechanical means to reduce the average particle size in the dispersion to less than 1000 nm." (Page 10, lines 14-25.) "As used herein, particle size refers to a number average particle size as measured by conventional particle size measuring techniques well known to those skilled in the art . . . By "an effective average particle size of less than about 1000 nm . . . (Page 16, lines 19-25.)
(iii) at least one surface modifier adsorbed on the surface of the crystalline therapeutic agent particles; and	having a surface modifier on the surface thereof; (Page 3, line 3.)
(b) administering said aerosol composition to the respiratory system of said mammal.	b) administering said aerosol to the respiratory system of said mammal. (Page 3, lines 4-5.)

As claim 28 is fully supported by the application, Applicants respectfully request withdrawal of this ground for rejection.

IV. Rejection of the Claims Under 35 U.S.C. § 103

A. Liversidge in view of Moren

Claims 28-40, 42-45, and 47-59 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Liversidge, U.S. Patent No. 5,145,684, in view of Moren, *Aerosols in Medicine, Principles, Diagnosis, and Therapy*, Elsevier Science Publisher, Chap. 13, pp. 321-350 (1993) ("Moren"). Specifically, the claims were rejected because "Liversidge et al. teaches the average particle size, surface modifier, and all other limitations of the presently claimed invention and Moren teaches aerosols and delivery to respiratory tract using poorly soluble drugs such as steroids" and therefore, it would have been obvious to one of skill in the art to prepare the method of delivering an aerosol to lungs by combining the teachings in these two

references for the treatment of respiratory diseases by using aerosols. Office Action at 4. Applicants respectfully traverse this ground for rejection.

To establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a), the Office must show: (1) at least a suggestion in the prior art of each element recited in the claim at issue, (2) some suggestion or motivation to have combined those elements, as proposed by the examiner, and (3) a reasonable expectation of success, likewise evidenced in the prior art, for the proposed combination. Furthermore, the Office must ascertain that the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made. As described below, the Office has not met this burden.

Moren describes some aqueous systems but teaches that one must choose a form of the drug that is soluble in water. See, Moren at section 4.1.1, page 340. Moren also describes alternative solubilization approaches for drugs that are not water soluble, including the use of cosolvents, solubilizing agents, and inclusion complexes (see Moren at 341). While at the end of section 4.1.1, Moren acknowledges that there may be cases where dissolution is not possible and that a suspension must be used, Moren also teaches that a number of factors need to be considered including investigation of physical stability and redispersion, dose accuracy, and the possible addition of surfactants and thickening agents which may influence the possibility of aerosolizing the liquid. *See* Moren at 341. Given Moren's teaching of various factors that must be considered when attempting to make an aerosol formulation of a poorly water-soluble drug, and that it is highly preferable to utilize water-soluble drugs in aerosol formulations, at the time the claimed invention was made **there was no reasonable expectation that attempts to make an aerosol formulation of a poorly water-soluble drug would be successful**. Rather, at best Moren is teaching that it may be "obvious to try" to make an aerosol of a poorly water-soluble drug. It has long been held, however, that "obvious to try" is not the standard of obviousness under 35 U.S.C. 103. *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210 (Fed. Cir. 1995). Thus, the Office has failed to establish a *prima facie* case of obviousness. Withdrawal of this ground for rejection is respectfully requested.

In addition, claim 44 is rejected because "Applicants have not shown how the method of treating various diseases is different from the prior art teaching by using their delivery method." Office Action at 4. But as stated above, the prior art does not describe the claimed delivery method, much less the various respiratory illnesses treated. As such, the method of claim 44 is distinct from the prior art teachings.

B. Liversidge in view of Gennaro and Kohler

Claims 28-40, 42-45, and 47-59 were also rejected under 35 U.S.C. 103(a) as allegedly obvious over Liversidge in view of Gennaro, *Remington's Pharmaceutical Sciences,* 17th Ed., Chap. 93, pp. 1670-1677 (1985) ("Gennaro"), and Kohler, *Aerosols in Medicine, Principles, Diagnosis, and Therapy*, Elsevier Science Publisher, Chap. 12, pp. 303-319 (1993) ("Kohler"). In particular, the claims were rejected because "Liversidge et al. teaches the average particle size, surface modifier, and all other limitations of the presently claimed invention[,] and Gennaro and Kohler references teach the use of aerosols for poorly soluble drugs and inhalation products and treatment of asthma and other respiratory illness[es]." Office Action at 6. Applicants respectfully traverse this ground for rejection.

Kohler generically describes aerosol formulations but is silent on the issue of inhaled particle size and does not give any indication that one would want to make a nanoparticulate formulation of a drug and aerosolize it. In fact, Kohler teaches away from aqueous aerosols containing drug nanoparticles. The last sentence on page 310 (before Figure 3) states that "the water solubility of the drug and its viscosity determine the amount of drug available in the aerosol droplet after nebulization." This statement implies that the drug must be in solution to be suitable for nebulization as an aqueous aerosol. Accordingly, one of skill in the art would not be motivated to combine Liversidge and Gennaro with the teachings in Kohler to make an aerosol formulation containing a nanoparticulate drug.

Gennaro describes compositions comprising propellants (but not water). There is some discussion of aerosolized suspensions, but in these cases the drug substance is

"insoluble in the propellant or propellant/solvent system." Gennaro at 1672. Gennaro's treatment of aqueous aerosols is limited to oil in water emulsions. Gennaro at 1673. Thus, Gennaro does not remedy the deficiencies of the teachings of Liversidge and Kohler to render the claimed invention obvious.

For at least these reasons, the claimed invention is patentable over the combination of cited references and, therefore, withdrawal of this ground for rejection is respectfully requested.

CONCLUSION

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and arguments.

The present application is now in condition for allowance. Early notice to that effect is earnestly solicited.

Examiner Qazi is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.